APPEAL BRIEF

Richard L. Catania, Esq.
Attorney for Appellants
Registration No. 32608

SCULLY SCOTT MURPHY & PRESSER, P.C.
400 Garden City Plaza, Suite 300
Garden City, New York 11530
(516) 742 4343
Customer No. 76701

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Applicants: Wayne D. Frasch, et al.

Examiner: Amanda Marie Shaw

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For: POLARIZATION-ENHANCED DETECTOR WITH GOLD NANORODS FOR DETECTING NANOSCALE ROTATIONAL MOTION AND METHOD THEREFORE

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Commissioner for Patents
P.O. Box 1450
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APPEAL BRIEF

Sir:

Pursuant to 35 U.S.C. §134 and 37 C.F.R §41.37, entry of this Appeal Brief in support of the Notice of Appeal filed November 10, 2008 in the above-identified matter is respectfully requested. This paper is submitted as setting forth the authorities and arguments upon which Appellants rely in support of the appeal from the Final Rejection dated July 11, 2008 rejecting Claims 40-59 in the above-identified patent application.

I. REAL PARTY IN INTEREST

The real party interest in the above-identified patent application is Arizona Board of Regents, Acting for and on behalf of Arizona State University; and Arizona Technology Enterprises, LLC.

II. RELATED APPEALS AND INTERFERENCES

No related pending appeals or interferences are known to Appellant.

III. STATUS OF CLAIMS

Claims 40-59 currently pend and are variously rejected under 35 USC 103(a).

Claims 40-59 are appealed. A clean copy of said claims is annexed in the Claims Appendix.

IV. STATUS OF AMENDMENTS

An amendment was filed after Notice of Appeal. Said amendment was submitted on April 3, 2009 under 37 CFR §41.33(a) to correct an objection to the specification.

V. SUMMARY OF CLAIMED SUBJECT MATTER

There are three independent claims in this appeal, Claims 40, 47 and 54 .

The invention with respect to independent Claim 40 comprises a method of detecting motion in nanoscale structures, comprising providing a molecular structure [see e.g. FIG 1, ELEMENT # 16] having a rotating arm [see e.g. FIG 1, #26]; attaching a nanoparticle [see e.g. FIG 1, #30] to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure, wherein the nanoparticle has a first surface and a second surface [see e.g. page 4, lines 25-34], and wherein the first surface has greater area than the second surface

[see e.g. page 8, lines 10-16]; exposing a light [see e.g. FIG 3, #38] to the nanoparticle, wherein a first surface of the nanoparticle scatters a first polarized wavelength of the light when the nanoparticle is in a first position [see e.g. page 8, lines 8-16] and a second surface of the nanoparticle scatters a second polarized wavelength of the light when the nanoparticle is in a second position [see e.g. page 8, lines 8-16]; and filtering the first and second wavelengths of the light through a polarizing filter to detect rotational motion by observing alternating first and second wavelengths of the light [see e.g. page 10, line 26-page 11, line 11].

The invention with respect to independent Claim 47 comprises a method of detecting motion in nanoscale structures comprising attaching a nanoparticle [see e.g. FIG 1, #16] to a rotating portion [see e.g. FIG 1, #26] of a molecular structure [see e.g. FIG 1, # 30], wherein the nanoparticle has a first surface and a second surface [see e.g. page 4, lines 25-34], and wherein the first surface has greater area than the second surface [see e.g. page 8, lines 10-16]; exposing a light [see e.g. FIG 3, #38] to a first surface of the nanoparticle to scatter a first polarized wavelength of the light [see e.g. page 8, lines 8-16]; exposing a light to a second surface of the nanoparticle to scatter a second polarized wavelength of the light [see e.g. page 8, lines 8-16]; and filtering the first and second wavelengths of the light using a polarizing filter to detect the rotational motion by observing the first and second wavelengths of the light [see e.g. page 10, line 26-page 11, line 11].

The invention with respect to independent Claim 54 comprises a method of detecting motion, comprising attaching an anisotropic nanoparticle [see e.g. 6, lines 12-15] to a rotating portion of a base structure [see e.g. FIG 1, #26]; exposing a light [see e.g. FIG 3, #38] to the anisotropic

nanoparticle to scatter first polarized and second polarized wavelengths of the light to detect the rotation motion by observing the first polarized and second polarized wavelengths of the light [see e.g. page 8, lines 8-16].

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. The rejection of Claims 40-45, 47-52 under 35 USC 103(a) as being obvious over Yasuda et al. "Resolution of Distinct Rotational Substeps by Submillisecond Kinetic Analysis" Nature, vol. 410, pp. 898-904, April 19, 2001 (**"Yasuda"**) in view of Sonnichsen et al. "Drastic Reduction of Plasmon Damping in Gold Nanorods" Physical Review Letters, vol. 88, No. 7, pp.077402-1 to -4, Feb. 18, 2002 (**"Sonnichsen"**) as evidenced by Mock et al. "Composite Plasmon Resonant Nanowires" Nano Letters, Vol. 2, No. 5, pp. 465-469, April 2002 (**"Mock"**) and in further view of US Patent No. 6449088 (**"Pettingell"**).

B. The rejection of Claims 54-59 under 35 USC 103(a) as obvious over Yasuda in view of Sonnichsen as evidenced by Mock.

C. The rejection of Claims 46 and 53 under 35 USC 103(a) as obvious over Yasuda in view of Sonnichsen as evidenced by Mock and Pettingell as applied to Claims 40 and 47, in further view of US Patent 6232066 (**"Felder"**).

VII. ARGUMENT

A. The rejection of Claims 40-45 and 47-52 under 35 USC 103(a) erroneously employs hindsight.

These claims relate to the detection of motion in nanoscale molecular structures having a rotating arm to which is attached a nanoparticle such as a gold nanorod. In the context of a nanorod for

purposes of present discussion only, when exposed to light, the first and second surfaces of the nanorod scatter first and second wavelengths of polarized light. By the method claimed, these are filtered to detect the rotation by observing the alternating wavelengths, e.g. as a blinking of red and green light. The method is concededly new inasmuch as no rejections under 35 USC 102 have been imposed. The question is whether this new invention is obvious over the art cited. Appellants submit it is not.

The obviousness rejection is first and foremost premised on the combination of Yasuda and Sonnichsen. The further use of Mock and Pettingell presupposes the propriety the initial combination. We turn to that initial combination.

Yasuda: explores the rotational substeps of F_1-ATPase enzyme, which can act as a rotary motor under certain conditions. To do so, Yasuda attaches a gold bead of 40 nm diameter to a unit of the enzyme, then captures images of the actual rotation by high speed CCD camera at 8000 frames per second. Motion of the bead is pictured as sequential images and measurements are made therefrom. See Yasuda, page 898-899 col. 1 and Figure 1.

One of Yasuda's concerns involves viscous friction. At page 898, col. 1, last six lines, it states:

> "Viscous friction imposed on the actin filament prevented fast rotation of F_1 and obscured the stepping behavior. Here we have used a smaller marker, a colloidal gold bead of 40-nm diameter, for which the viscous friction is 10^{-3} to 10^{-4} times that for actin (Fig. 1b). In the resultant high-speed rotation, we are able to resolve substeps."

Then at Figure 1b, the text for same states:

> "The 40-nm bead gave a large enough optical signal that warranted a submillisecond resolution; but the bead was small enough not to impede the rotation."

Thus, Yasuda requires a bead of sufficiently small size so as to not impede rotation, yet large enough to give an optical signal measurable by Yasuda's technique. What is that technique?

Yasuda uses a laser to illuminate the specimen containing the rotating gold bead under dark field microscopy. The light scattered by the gold bead as it turns is photographed by a fast frame CCD camera. The pictures captured are then analyzed for centroid rotation. See Yasuda Figure 1, page 899 col. 1, and page 903 "Microscopy" et seq.

This is unlike the present invention. Unlike Yasuda's gold bead, the nanoparticle of the invention is exemplified by a gold nanorod. That is, it is a particle that has first and second surfaces, wherein the first surface is of greater area than the second. It is anisotropic. This feature permits an entirely different approach to detecting motion. Rather than capturing sequential images of the particle *per se* as it rotates, as in Yasuda, the particle in the present invention scatters polarized light at first and second wavelengths which correspond to the first and second surfaces as they rotate. When detected through a polarizing filter, the motion is observed as a flashing, or blinking of different colors of light, e.g. red and green.

These differences are recognized by the rejection of record. However, it is officially alleged that Sonnichsen provides curative disclosure under 35 USC 103. But an assessment of Sonnichsen shows (i) that it is directed to sufficiently different art and would not be looked to in the first instance; and (ii) that the combination that would objectively result would not harken to the invention, but would instead dovetail directly into Yasuda's self-expressed concerns of friction and impedance and brightness, and in doing so would use the very same fast frame imaging as originally described.

It is Appellants' contention that only by having the benefit of the inventive disclosure in hand would the tortuous combined construct of Yasuda and Sonnichsen of the rejection be possible. We turn now to Sonnichsen.

Sonnichsen: relates to plasmon damping of gold nanoparticles, including beads and rods. Plasmon damping is of particular concern in surface-enhanced Raman scattering (SERS), which requires the dephasing of the particle plasmon to be slow. Sonnichsen reports that the dephasing rate for nanorods is reduced as compared to nanospheres and concludes that the rods would be superior to spheres in "optical applications where large local field enhancements are required, such as SERS." See Sonnichsen at page -77402-1, cols. 1 and 2, and page 77402-4 col. 1 bridging col. 2.

(i) Sonnichsen is non-analogous to Yasuda and the present invention:
Sonnichsen is not directed to rotational motion or the detection of same. Quite the opposite. It is directed to SERS, which is a static mode of analysis, and like optical applications. The rejection of record urges that the broad term "optical applications" necessarily invokes motion detection of the type to which the present invention relates. But Sonnichsen itself describes these as "optical applications where absorptive losses, sample heating, or quenching of fluorescence from absorbed molecules need to be avoided," page 077402-4 col. 1, middle paragraph. Rotation and motion detection are wholly unmentioned.

Indeed, SERS is typically employed to study monolayers of materials absorbed on metal surfaces: a static environment. To be sure, Sonnichsen studies the very nanorods alleged to be substitutable with Yasuda under static conditions. The rods are spin casted in solution onto glass slides whereupon they are subjected to Transmission Electron Microscopic (TEM) study. No rotation occurs. No assessment of rotational behavior of any kind –let alone polarized scattering and corresponding differential wavelength detection under these conditions —is described. And no suggestion of these properties is reasonably and objectively hinted at by Sonnichsen. Sonnichsen is directed to applications sufficiently disparate from that claimed so as to be non-

analogous in the first instance, and the rejections employing it should be overturned on this appeal accordingly.

But even assuming *pro arguendo* that Sonnichsen was viably analogous, the result of its pairing with Yasuda clearly and unambiguously suggests something other than the invention, as alleged in the rejection. We indulge the combination as follows without prejudice to the foregoing position:

<u>(ii) The combination of Yasuda and Sonnichsen does not objectively lead to the invention:</u> Among other things, Sonnichsen makes the following conclusion about the dephasing attributable to nanorods (page 077402-4, penultimate paragraph):

> "These findings result in relatively high light-scattering efficiencies and large local-field enhancement factors, making nanorods interesting for a range of optical applications."

What does this mean as a practical matter? Sonnichsen gives us an example (*ibid*, middle of col. 1):

> "...our observation that the rods appear as bright in the microscopic measurement as spheres of much larger volume..."

Lets now combine this with Yasuda. As before stated, Yasuda worries over having a particle that is sufficiently large so as to scatter enough light to create an image that can be captured, while at the same time having a particle that is sufficiently small so as to not impede rotation. Yasuda chooses a 40-nm bead. Sonnichsen provides another solution to this problem. As quoted directly above, Sonnichsen teaches that the nanorods are brighter than spheres of much larger volume. One reading this in the context of Yasuda would reasonably and objectively conclude that one could indeed use the nanorods of Sonnichsen in Yasuda for the latter's high speed imaging.

That is, one would replace the gold nanobead of Yasuda with a gold nanorod of Sonnichsen for the reasons expressed in Sonnichsen, to wit: one could reduce the size relative to a bead, and thereby address Yasuda's one concern over impeding rotation, while concomitantly manifest sufficient if not improved brightness needed for capture by the CCD imaging, and thereby address Yasuda's other concern about optical signal. In other words, one can combine the references commensurate with the confines of those same references, and come to an end configuration that is wholly consistent with the needs and teachings of those references -- all without having to undertake a wholesale modification of the imaging technique as the rejection would have it.

Indeed, there is not only no need to revamp Yasuda's imaging technique so as to take advantage of anisotropic scattering and detection using polarized filtering that attends gold nanorods under the conditions of the invention, there is no reasonable suggestion that such properties obtain, and no motivation to do so. The Final Rejection avers that the excitation light in Sonnichsen is polarized and states in conclusory fashion that the scattered light is polarized and can therefore be detected as claimed. But this is gleaned from Appellants' specification. Appellants find no such disclosure in Sonnichsen to support this proposition, and urge on this appeal that it is only arrived at when viewed with improper hindsight using the instant specification as a guide.

Appellants submit that the combination of Yasuda and Sonnichsen does not suggest the invention claimed; that the combination that results, given the very parameters of those references, inexorably leads to the Yasuda configuration and CCD imaging technique, only now with a nanorod for the purposes stated in Sonnichsen: smaller size for reduced reduced impedance with maintained brightness for high speed imaging. The invention as claimed is not implicated.

As cautioned by the U.S. Supreme Court in KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385, 1397 (2007):

> "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning. See *Graham*, 383 U.S., at 36 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to " 'guard against slipping into the use of hindsight' "

Appellants respectfully submit that such is the situation here. That, to the extent Yasuda and Sonnichsen are combinable, they are so for the purpose Appellants have articulated above. To go further, as in the rejections, and supplant the entirety of Yasuda's detection scheme, replacing it with one far different when there is no necessity to do so, distorts the teachings of those references and bespeaks a lack of motivation and a hindsight appreciation of Appellants' invention. As aptly noted in In re Fritch, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992):

> "The mere fact that the prior art may be *modified* in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. [The references]...fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner..." (emphasis in original; citation omitted).

The references to Mock and Petingell when added to the mix do not alter this outcome. Mock investigates plasmon resonance of nanowires. The Final Rejection employs Mock for the purpose of allegedly showing various polarization properties of various metallic nanoparticles under various conditions. But the proper combination of Yasuda and Sonnichsen as postulated above has no need for polarized considerations in order to operate and create its CCD image. Mock does not change this and, in fact, corroborates the hindsight evaluation that has been used, for only with the inventive disclosure on full display would one ever think to look at polarization and Mock. Pettingell is even farther removed, and deals with the details of polarizing filters and

the like. Again, these references are come to *a posteriori* for features that arise only on the incorrect legal assumption that the principal combination of Yasuda and Sonnichsen invokes the claims under 35 USC 103(a).

As demonstrated above, the primary combination does not lead to, require, or suggest polarized detection; indeed the primary combination has no need for it; hence, these additional references do not render the claims obvious.

Appellants hereby respectfully request reversal and withdrawal of the rejection of Claims 40-45 and 47-52 under 35 USC 103 and a finding of non-obvious for same over the art cited.

<u>B. The rejection of Claims 54-59 under 35 USC 103(a) also erroneously employs a hindsight reconstruction:</u>

These claims specify the particle as anisotropic in the first instance (Claim 54) whereupon it is preferably rod-shaped with first and second surfaces (Claims 55-57) and correspondingly scattered polarized wavelengths which are detected, including preferably as red and green light (Claims 58-59).

The combination of Yasuda and Sonnichsen as evidenced by Mock is cited to support the rejection. Appellants have fully addressed the combination of these references in their argument hereinabove in Section VI-A in relation to Claims 40-45 and 47-52 and incorporate these here in full. In short: Yasuda plus Sonnichsen lead to the configuration of Yasuda only now with a Sonnichsen nanorod, imaged by the CCD camera of Yasuda for purposes of reduced particle size in answer to impedance concerns, while maintaining sufficient optical signal for fast frame imaging.

Appellants hereby respectfully request reversal and withdrawal of the rejection of Claims 54-59 under 35 USC 103 and a finding of non-obvious for same over the art cited.

C. The rejection of Claims 46 and 53 under 35 USC 103(a) continues the use of hindsight and is in error:

These claims employ a DNA detection strand between the nanoparticle (e.g. nanorod) and the molecular structure (e.g. F_1-ATPase enzyme). They have been rejected as obvious under the combination of Yasuda, Sonnichsen, Mock, Pettingell –all as discussed in Section VI-A and Claims 40-47 and 47-52, the totality of which is incorporated herein by reference-- and Felder. Felder is relied upon for its ostensible teaching of anchor oligonucleotides and linkers. It is relied upon for this specific feature and does not bring the principal combination of Yasuda and Sonnichsen any closer to the claimed invention, nor does it suggest the deficiencies of same vis-à-vis the claims. Like Mock and Pettingell, it presupposes the predicate combination, as alleged in the rejections, is correct, which combination Appellants dispute and have shown to be not the case given a rigorous reading of the art.

Appellants hereby respectfully request reversal and withdrawal of the rejection of Claims 46 and 53 under 35 USC 103 and a finding of non-obvious for same over the art cited.

Respectfully Submitted,

Richard L. Catania

Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, New York 11530
Customer No. 76701

VIII. CLAIMS APPENDIX

40. (REJECTED) A method of detecting motion in nanoscale structures, comprising:

providing a molecular structure having a rotating arm;

attaching a nanoparticle to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure, wherein the nanoparticle has a first surface and a second surface, and wherein the first surface has greater area than the second surface;

exposing a light to the nanoparticle, wherein a first surface of the nanoparticle scatters a first polarized wavelength of the light when the nanoparticle is in a first position and a second surface of the nanoparticle scatters a second polarized wavelength of the light when the nanoparticle is in a second position;

filtering the first and second wavelengths of the light through a polarizing filter to detect rotational motion by observing alternating first and second wavelengths of the light.

41. (REJECTED) The method of Claim 40 wherein the nanoparticle is rod-shaped.

42. (REJECTED) The method of Claim 41 wherein the nanoparticle is a gold nanorod.

43. (REJECTED) The method of Claim 42 wherein the first polarized wavelength of the light is longer than the second polarized wavelength of the light.

44. (REJECTED) The method of Claim 43 wherein the first polarized wavelength of the light is red light and the second polarized wavelength of the light is green light.

45. (REJECTED) The method of Claim 40 wherein the molecular structure is an F1-ATPase enzyme.

46. (REJECTED) The method of Claim 40 further including the step of disposing a detection DNA strand between the nanoparticle and the molecular structure, wherein the detection DNA

strand hybridizes with a target DNA strand, if the target DNA strand matches the detection DNA strand, to form a structural link between the molecular structure and the nanoparticle.

47. (REJECTED) A method of detecting motion in nanoscale structures comprising:

attaching a nanoparticle to a rotating portion of a molecular structure, wherein the nanoparticle has a first surface and a second surface, and wherein the first surface has greater area than the second surface;

exposing a light to a first surface of the nanoparticle to scatter a first polarized wavelength of the light;

exposing a light to a second surface of the nanoparticle to scatter a second polarized wavelength of the light; and

filtering the first and second wavelengths of the light using a polarizing filter to detect the rotational motion by observing the first and second wavelengths of the light.

48. (REJECTED) The method of Claim 47 wherein the nanoparticle is rod-shaped.

49. (REJECTED) The method of Claim 48 wherein the nanoparticle is a gold nanorod.

50. (REJECTED) The method of Claim 49 wherein the first polarized wavelength of the light is longer than the second polarized wavelength of the light.

51. (REJECTED) The method of Claim 50 wherein the first polarized wavelength of the light is red light and the second polarized wavelength of the light is green light.

52. (REJECTED) The method of Claim 47 wherein the molecular structure is an F1-ATPase enzyme.

53. (REJECTED) The method of Claim 47 further including the step of disposing a detection DNA strand between the nanoparticle and the molecular structure, wherein the detection DNA

strand hybridizes with a target DNA strand, if the target DNA strand matches the detection DNA strand, to form a structural link between the molecular structure and the nanoparticle.

54. (REJECTED) A method of detecting motion, comprising:

attaching an anisotropic nanoparticle to a rotating portion of a base structure;

exposing a light to the anisotropic nanoparticle to scatter first polarized and second polarized wavelengths of the light to detect the rotation motion by observing the first polarized and second polarized wavelengths of the light.

55. (REJECTED) The method of Claim 54 wherein the anisotropic nanoparticle is rod-shaped.

56. (REJECTED) The method of Claim 55 wherein the anisotropic nanoparticle is a gold nanorod.

57. (REJECTED) The method of Claim 55 wherein the anisotropic nanoparticle has a first surface and a second surface, and wherein the first surface has greater area than the second surface.

58. (REJECTED) The method of Claim 55 wherein the first polarized wavelength of the light is longer than the second polarized wavelength of the light.

59. (REJECTED) The method of Claim 58 wherein the first polarized wavelength of the light is red light and the second polarized wavelength of the light is green light.

IX. Evidence Appendix

None.

X. Related Proceedings Appendix

None.